

REMARKS/ARGUMENTS

In order to expedite prosecution, Applicants have revised claims 13-22. Claim 13 has been limited to a contrast agent which targets the estrogen receptor. In addition, the vector (V) in claim 13 has been limited to an organic, drug-like small molecule. Basis can be found in the specification at page 10 line 23; page 12 line 23 to page 13 line 4; plus page 18 line 10 to page 19 line 7; as well as Example 3 and previous claim 16. Claim 13 has also been amended to require that the contrast agent is fluorescent. Basis can be found at page 14 lines 3 to 4.

Claims 16 and 17 have consequently been cancelled. Claims 13-15, 19-20 and 22 are therefore still pending.

1. CLAIM REJECTIONS: DOUBLE PATENTING.

Applicants note this provisional rejection over co-pending applications 10/573606, 10/582679, 10/582680, 10/582842 and 10/582893.

Applicants believe that the present amendment limiting to a specific biological target (estrogen) for optical imaging of endometriosis, now distinguishes the subject matter, so that this provisional rejection no longer applies. In the event, however, that the rejection is maintained and the present claims are allowed, Applicants will consider filing a terminal disclaimer as necessary.

2. CLAIM REJECTIONS: 35 USC §112.

Claims 13-17, 19, 20-22 stand rejected as failing to comply with the written description requirement under 35 USC §112, first paragraph.

Applicants stress that claim 13 is now limited to estrogen as the biological target and a drug-like small molecule as the vector. It is believed that the specification at page 10 line 23; page 12 line 23 to page 13 line 4; plus page 18 line 10 to page 19 line 7; as well as Example 3 demonstrates that applicants were in possession of the claimed invention.

The revised claims are therefore believed to comply with 35 USC §112, and Applicants contend that this rejection should be withdrawn.

3. CLAIM REJECTIONS: 35 USC §103.

3.1 Weissleder and Schneider.

Claims 13-17, 19, 20 and 22 stand rejected as lacking an inventive step over Weissleder in view of Schneider.

The Examiner's logic was that Weissleder provides optical probes for imaging cathepsin, and that Schneider teaches that cathepsin S is upregulated in endometriosis. The logical combination was therefore argued to be the use of the probes of Weissleder in the optical imaging of endometriosis – leading to subject matter within the scope of previous claim 13.

Applicants contend that this logic is no longer valid, since revised 13 is limited to estrogen as the biological target, and both Weissleder and Schneider are silent on estrogen. The inventive step attack based on the combination of those two references should therefore be withdrawn.

4. NEW GROUNDS FOR REJECTION.

4.1 Smith and Weissleder.

Claims 13-17, 19, 20 and 22 stand rejected as lacking an inventive step over Smith (US 2004/0053823) and Weissleder.

The Examiner discloses that the person skilled in the art would employ the NIRF probes of Weissleder with the MMP-targeting peptides of Smith.

Applicants point out that the peptides of Smith target MMP-2, MMP-9 and MT1-MMP. Such targeting is outside the scope of revised claim 13. Hence, no combination of Smith and Weissleder could lead to claim 13. Consequently, the objection based on the Smith/Weissleder combination should be withdrawn.

4.2 Fevig, Wallace and Weissleder.

Claims 13-17, 19, 20 and 22 stand rejected as lacking an inventive step over Fevig in view of Wallace, and further in view of Weissleder.

The Examiner's logic (page 13) is that the person skilled in the art would:

"...provide the compounds of Fevig for imaging of additional tumor tissues in additional to breast tumor, such as endometriosis..."

and later on:

"...for imaging estrogen receptor positive cancers, such as endometriosis..."

Applicants refer to the present specification at page 1 lines 15 to 30:

"The disorder is characterized by endometrial tissue being present in other organs than the endometrium."

Applicants also refer to the Wikipedia definition:

"Endometriosis (from *endo*, "inside", and *metra*, "womb") is a medical condition in women in which endometrial like cells appear and flourish in areas outside the uterine cavity. The uterine cavity is lined by endometrial cells, which are under the influence of female hormones. These endometrial-like cells in areas outside the uterus (endometriosis) are influenced by hormonal changes and respond similarly as do those cells found inside the uterus. Symptoms often worsen in time with the menstrual cycle.

Endometriosis is typically seen during the reproductive years; it has been estimated that it occurs in roughly 5% to 10% of women. Symptoms may depend on the site of active endometriosis. Its main but not universal symptom is pelvic pain in various manifestations. Endometriosis is a common finding in women with infertility."

Hence, Applicants respectfully point out that endometriosis is not a cancerous condition.

The Examiner's combination is to adapt the agents taught by Fevig, for the broader range of disease states taught by Wallace, whilst adopting the optical probes taught by Weissleder.

Applicants refer to revised claim 13, where the optical contrast agent is required to be fluorescent when administered to the animate subject. By definition that means that the agent is not quenched. Applicants also refer to the present specification at page 15 lines 14 to 18, where such probes are described as a further aspect. That embodiment corresponds to the activatable probe approach of Weissleder, wherein enzyme activation *in vivo* turns a non-fluorescent (i.e. quenched) probe into a fluorescent probe only after enzyme cleavage *in vivo*. It is not, however, claimed - since the term 'quencher' does not appear in the present claims. Hence, applicants contend that is consistent with the above – i.e. that activatable probes are outside the scope of present revised claim 13.

Claim 13 now requires that the agent administered is already fluorescent. That is totally different from the teaching of Weissleder, where a quenched probe is administered. The combination suggested by the Examiner therefore teaches towards subject matter which is outside the scope of revised claim 13. The inventive step objection based on the Fevig/Wallace/Weissleder combination should therefore also be withdrawn.

CONCLUSION.

Applicants respectfully hold that the claims submitted herewith fulfill the requirements of a patentable invention and that all rejections and objections be withdrawn and claims 13-15, 19-20 and 22 be allowed.

The Examiner is invited to telephone the undersigned in order to resolve any issues that might arise and to promote the efficient examination of the current application.

Respectfully submitted,

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